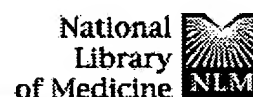


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DATE: Monday, July 14, 2003

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<i>DB=DWPI; PLUR=YES; OP=ADJ</i>			
L3	Blake J.in. and virus	4	L3
L2	Blake J.in.	188	L2
L1	Choppin J.in.	4	L1

END OF SEARCH HISTORY



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- ☐ 1: [Bourgault Villada I, Beneton N, Bony C, Connan F, Monsonego J, Bianchi A, Saiag P, Levy JP, Guillet JG, Choppin J.](#) [Related Articles, Links](#)

Identification in humans of HPV-16 E6 and E7 protein epitopes recognized by cytolytic T lymphocytes in association with HLA-B18 and determination of the HLA-B18-specific binding motif.

Eur J Immunol. 2000 Aug;30(8):2281-9.

PMID: 10940919 [PubMed - indexed for MEDLINE]

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- ☐ 2: [Ressing ME, Sette A, Brandt RM, Ruppert J, Wentworth PA, Hartman M, Oseroff C, Grey HM, Melief CJ, Kast WM.](#) [Related Articles, Links](#)

Human CTL epitopes encoded by human papillomavirus type 16 E6 and E7 identified through in vivo and in vitro immunogenicity studies of HLA-A*0201-binding peptides.

J Immunol. 1995 Jun 1;154(11):5934-43.

PMID: 7538538 [PubMed - indexed for MEDLINE]

Related Resources

- ☐ 3: [Bauer M, Wagner H, Lipford GB.](#) [Related Articles, Links](#)

HPV type 16 protein E7 HLA-A2 binding peptides are immunogenic but not processed and presented.

Immunol Lett. 2000 Jan 10;71(1):55-9.

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Synthetic peptides induce a cytotoxic response against human papillomavirus type-18.

Gynecol Oncol. 2001 Jul;82(1):77-83.













PMID: 11426965 [PubMed - indexed for MEDLINE]








- ☐ 5: [Bauer S, Heeg K, Wagner H, Lipford GB.](#) [Related Articles, Links](#)


Identification of H-2Kb binding and immunogenic peptides from human papilloma virus tumour antigens E6 and E7.

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[HLA-A2-restricted peripheral blood cytolytic T lymphocyte response to HPV type 16 proteins E6 and E7 from patients with neoplastic cervical lesions.](#)
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-  **7:** [Evans M, Borysiewicz LK, Evans AS, Rowe M, Jones M, Gileadi U, Cerundolo V, Man S.](#) [Related Articles, Links](#)
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-  **9:** [Nakagawa M, Stites DP, Farhat S, Sisler JR, Moss B, Kong F, Moscicki AB, Palefsky JM.](#) [Related Articles, Links](#)
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-  **10:** [Yoon H, Chung MK, Min SS, Lee HG, Yoo WD, Chung KT, Jung NP, Park SN.](#) [Related Articles, Links](#)
 [Synthetic peptides of human papillomavirus type 18 E6 harboring HLA-A2.1 motif can induce peptide-specific cytotoxic T-cells from peripheral blood mononuclear cells of healthy donors.](#)
Virus Res. 1998 Mar;54(1):23-9.
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-  **11:** [Ressing ME, van Driel WJ, Celis E, Sette A, Brandt MP, Hartman M, Anholts JD, Schreuder GM, ter Harmsel WB, Fleuren GJ, Trimbos BJ, Kast WM, Melief CJ.](#) [Related Articles, Links](#)
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-  **12:** [Nimako M, Fiander AN, Wilkinson GW, Borysiewicz LK, Man S.](#) [Related Articles, Links](#)
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-  **18:** [Thornburg C, Boczkowski D, Gilboa E, Nair SK.](#) [Related Articles, Links](#)
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J Immunother. 2000 Jul-Aug;23(4):412-8.
PMID: 10916750 [PubMed - indexed for MEDLINE]
-  **19:** [Feltkamp MC, Smits HL, Vierboom MP, Minnaar RP, de Jongh BM, Drijfhout JW, ter Schegget J, Melief CJ, Kast WM.](#) [Related Articles, Links](#)
Vaccination with cytotoxic T lymphocyte epitope-containing peptide protects against a tumor induced by human papillomavirus type 16-transformed cells.
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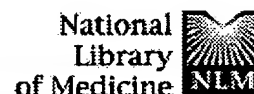
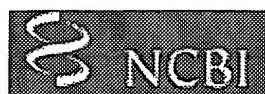
Induction of specific CD8+ T-lymphocyte responses using a human papillomavirus-16 E6/E7 fusion protein and autologous dendritic cells.
Cancer Res. 1999 Mar 15;59(6):1184-7.
PMID: 10096544 [PubMed - indexed for MEDLINE]

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☐ 1: Virus Res. 1998 Mar;54(1):23-9.

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Synthetic peptides of human papillomavirus type 18 E6 harboring HLA-A2.1 motif can induce peptide-specific cytotoxic T-cells from peripheral blood mononuclear cells of healthy donors.

PubMed Services

Yoon H, Chung MK, Min SS, Lee HG, Yoo WD, Chung KT, Jung NP, Park SN.

Virus/Oncology Research Unit, Korea Research Institute of Bioscience and Biotechnology, KIST, Yusong, Taejeon, South Korea.

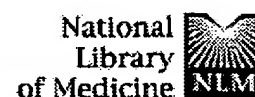
Related Resources

To identify cytotoxic T-cell (CTL) epitopes against human papillomavirus type 18 (HPV 18) E6 protein that might be useful for developing peptide-based vaccine against HPV 18 infection, 18 peptides which possibly contain CTL epitopes were selected on the basis of previously described human leukocyte antigen (HLA)-A2.1-binding motif and chemically synthesized. In the binding assay of the synthetic peptides, 8 out of 18 synthetic peptides enhanced the expression of HLA-A2.1 molecules on T2 cell surface, which implies that these peptides were able to bind the HLA molecules. Those peptides having good binding affinity to HLA-A2.1 were tested for their ability to activate CTLs which were isolated from peripheral blood mononuclear cells (PBMCs) of healthy blood donors and to kill the target T2 cells pulsed with the same peptide. Five out of eight tested peptides activated CTLs and killed the target cells.

PMID: 9660068 [PubMed - indexed for MEDLINE]

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Identification in humans of HPV-16 E6 and E7 protein epitopes recognized by cytolytic T lymphocytes in association with HLA-B18 and determination of the HLA-B18-specific binding motif.

PubMed Services

Bourgault Villada I, Beneton N, Bony C, Connan F, Monsonogo J, Bianchi A, Saia P, Levy JP, Guillet JG, Choppin J.

Institut Cochin de Genetique Moleculaire, Laboratoire d'Immunologie des Pathologies Infectieuses et Tumorales, INSERM U445, Universite Rene Descartes, Hopital Cochin, Paris, France. bourgault@cochin.inserm.fr

Related Resources

Human papilloma virus type 16 (HPV-16) is the HPV most frequently associated with cervical carcinoma in humans. For the prevention or treatment of cervical carcinoma, the E6 and E7 oncoproteins appear to be good targets for vaccine-induced cytotoxic T lymphocytes (CTL). Lipopeptide vaccination is an efficient way of stimulating cellular responses. However, to synthesize effective lipopeptides, it is necessary to define which epitopes are immunogenic. In this study we first determined that peptide 80 - 88 of the E6 protein was recognized by CTL from a healthy donor in association with the HLA-B18 molecule. We then defined the HLA-B18 anchoring peptide motif by testing the binding of various short peptides with the HLA-B18 molecule and showed that it was related to the HLA-A1-specific peptide motif. Furthermore, in analyzing the potential E7 epitopes susceptible to associating with HLA-B18, we demonstrated that peptide E7 44 - 52 gave the strongest binding. It could also be recognized by CTL from peripheral blood mononuclear cells (PBMC) of the same healthy donor. Finally, with PBMC from a patient with a cervical intraepithelial neoplasia grade 3, we found CTL which recognized the E6 80 - 88 epitope. We have hence identified two peptides encoded by the E6 and E7 proteins which are presented by the HLA-B18 molecule and could be included in a vaccine against HPV-16.

PMID: 10940919 [PubMed - indexed for MEDLINE]



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Human CTL epitopes encoded by human papillomavirus type 16 E6 and E7 identified through in vivo and in vitro immunogenicity studies of HLA-A*0201-binding peptides.

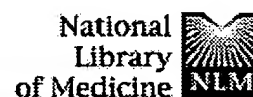
PubMed Services

Ressing ME, Sette A, Brandt RM, Ruppert J, Wentworth PA, Hartman M, Oseroff C, Grey HM, Melief CJ, Kast WM.

Department of Immunohematology and Blood Bank, University Hospital Leiden, The Netherlands.

Related Resources

Human papillomavirus type 16 (HPV16) is strongly associated with cervical carcinogenesis. The HPV16 E6 and E7 oncoproteins are constitutively expressed in the majority of cervical tumor cells and are, therefore, attractive targets for CTL-mediated immunotherapy. In mice, the outgrowth of a lethal dose of HPV16-induced tumor cells has been prevented by vaccination with a CTL epitope encoded by HPV16 E7, indicating the feasibility of peptide immunization to obtain antitumor CTL responses. In the present study, the immunogenicity of 9 HLA-A*0201-binding peptides encoded by HPV16 E6 and E7 was analyzed in vivo in HLA-A*0201Kb transgenic mice and in vitro in CTL cultures induced from PBMC of HLA-A*0201+ healthy donors. Four peptides with a good binding affinity were immunogenic in HLA-A*0201Kb transgenic mice, and three of them were also highly immunogenic in CTL induction experiments with PBMC of HLA-A*0201+ healthy donors. Human CTL clones specific for these three peptides were capable of lysing the HPV16 E7-containing HLA-A*0201+ cervical carcinoma cell line CaSki. These E7-derived peptides (11-20, YMLDLQPETT; 82-90, LLMGTLGIV; 86-93, TLGIVCPI), therefore, are likely to represent naturally processed human CTL epitopes of HPV16. Additionally, these three HPV16-encoded peptides have the highest affinity of binding to the HLA-A*0201 molecule. In this study, peptides with a lower binding affinity were less immunogenic. Therefore, our data illustrate that the HLA-binding affinity of a peptide has a major impact on its immunogenicity. In conclusion, we have identified immunogenic peptides encoded by HPV16 E6 and E7 that could be used in vaccines for the prevention and treatment of cervical carcinoma.



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HPV type 16 protein E7 HLA-A2 binding peptides are immunogenic but not processed and presented.

Bauer M, Wagner H, Lipford GB.

PubMed Services

Institute of Medical Microbiology, Immunology and Hygiene, Munich, Germany.

Related Resources

Human papillomaviruses (HPV) have been implicated in the etiology of cervical malignancies and a high percentage of cervical carcinoma cells express HPV-16 E6 and E7 oncoproteins. These proteins are attractive targets for cytolytic T lymphocyte (CTL) mediated immunotherapy. We screened peptides derived from the HPV-16 E7 protein for binding to HLA-A2 and tested their potential to induce specific CTL responses in chimeric HLA-A2/H2-Kb transgenic mice. From eight potential binding peptides four displayed binding and were tested for immunogenicity. CTL activity was tested using target cells pulsed with peptide or expressing E7 protein. While there was no CTL induction observed with the peptides 7-15, 66-74 and 82-90, CTL from mice immunized with 86-93 lysed targets presenting the peptide in the context of the HLA-A2/H2-Kb molecule or wild-type HLA-A2. In contrast, 86-93 induced CTL showed no cytolytic activity against cells expressing the protein E7 and vaccination with the E7 protein did not lead to cytotoxicity against targets pulsed with the 86-93 peptide. Therefore the peptide 86-93, which binds to HLA-A2, is able to induce CTL responses in context of HLA-A2, but the peptide appears not to be processed or presented by HPV type 16 infected cells.

PMID: 10709786 [PubMed - indexed for MEDLINE]

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☐ 1: Scand J Immunol. 1995 Sep;42(3):317-23.

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Identification of H-2Kb binding and immunogenic peptides from human papilloma virus tumour antigens E6 and E7.

Bauer S, Heeg K, Wagner H, Lipford GB.

PubMed Services

Institute for Medical Microbiology, Technical University of Munich, Germany.

Related Resources

Peptides can be used to induce MHC class I restricted cytotoxic T cells (CTL) through in vivo immunization. This approach may enable the development of peptide vaccination schemes for immunization against viral infection in humans. Human papillomavirus (HPV) is one of a few viruses associated with human cancer and the development of an anti-cancer vaccine seems possible. As a model approach, we searched the E6 and E7 proteins of the human papillomavirus type 16 for possible murine MHC class I restricted peptide epitopes. We utilized the mouse H2-Kb peptide binding motif which consists of phenylalanine or tyrosine at position five and leucine at the carboxy-terminus with the modification that leucine could be replaced by other aliphatic but non-aromatic amino acids. Four peptide sequences from E6 and two from E7 were selected. These peptides were tested for their ability to bind and stabilize Kb and for their immunogenicity in vivo. It was shown that one peptide from E6, E6.1 (50-57), bound Kb, but was not able to prime mice in vivo. In contrast, the two selected E7 peptides E7.1 (21-28) and E7.2 (48-55) bound Kb and were immunogenic in vivo. The peptide induced CTL lysed syngeneic EL-4 cells transfected with the open reading frame of E7 but not vector only transfectants. This implies that both peptides were naturally processed and presented by Kb on the surface of target cells. MHC class I peptide binding motifs therefore appear to be an effective and useful tool to predict peptide epitopes of proteins associated with cancer.

PMID: 7660065 [PubMed - indexed for MEDLINE]

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Dec 8, 2000

DERWENT-ACC-NO: 2001-064175

DERWENT-WEEK: 200108

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TITLE: New polyepitopic fragments from human papilloma virus E6 and E7 proteins, useful for treatment or prevention of e.g. cervical neoplasia and cancer

INVENTOR: BOURGAULT, V I; CHOPPIN, J ; CONNAN, F ; FERRIES, E ; GUILLET, J G

PRIORITY-DATA: 1999FR-0007012 (June 3, 1999), 1999FR-0012511 (October 7, 1999)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
FR 2794371 A1	December 8, 2000		027	A61K039/12

INT-CL (IPC): A61 K 39/12; A61 K 39/42; A61 K 48/00; A61 P 31/20; A61 P 35/00; C07 K 14/025; C07 K 16/08; C12 N 15/37

ABSTRACTED-PUB-NO: FR 2794371A

BASIC-ABSTRACT:

NOVELTY - Polyepitopic fragments (I) from the E6 and E7 proteins of human papilloma virus (HPV), are new.

DETAILED DESCRIPTION - Polyepitopic fragments (I) from the E6 and E7 proteins of human papilloma virus (HPV), are new. (I) is contained within any of the sequences:

ArgProArgLysLeuProGlnLeuCysThrGluLeuGlnThrThrIleHisAspIleIleLeu-

GluCysValTyrCysLysGlnGlnLeu;

ArgArgGluValTyrAspPheAlaPheArgAspLeuCysIleValTyrArgAspGlyAsn-

ProTyr;

IleSerGluTyrArgHisTyrCysTyrArgLeuTyrGlyThrThrLeuGluGlnGlnTyrAsn-

LysProLeuCysAspLeuLeuIle;

CysProGluGluLysGlnArgHisLeuAspLysLysGlnArgPheHisAsnIleArgGlyArg-

Trp;

GlyGlyAspThrProThrLeuHisGluTyrMetLeuAspLeuGlnProGluThrThrAspLeu-

TyrCysTyrGlnAlaGluProAspArgAlaHisTyrAsnIleValThrPheCysCysLys; and

LeuGlnAspLeuLeuMetGlyThrLeuGlyIleValCysProIleCysSerGlnLys.

These represent, respectively, amino acids 15-44, 46-67, 80-108 or 118-139 of E6 or 2-25, 44-60 or 79-97 of E7, and bind stably to, respectively, the human leukocyte antigen (HLA) type molecules A2, A11, A29, B7, B8, B35, B44 or B51; A2, A3, A11, A24, A29, B7, B27, B35, B44 or B51; A1, A3, A11, A24, A29, B7, B18, B35, B44 or B51; A24, B8, B18, B27, B35, B44 or B51; A1, A2, B18, B35, B44 or B62; A1, A3, A11, A29, B7, B18, B35, B44 or B51; or A2, A3, A11, A29 or B44. Alternatively, (I) comprises their

derivatives which bind to the same HLA molecules as the parent compounds, formed by substitution, deletion and/or addition of one or more amino acids, modification of at least one peptide bond (particularly replacement by retro or retro-inverso bonds) and/or substitution of at least one amino acid by a non-proteinogenic amino acid.

INDEPENDENT CLAIMS are also included for the following:

- (1) nucleic acid (II) that encodes (I) or its derivatives;
- (2) mono- or poly-clonal antibodies (Ab) directed against (I) or its derivatives; and
- (3) pharmaceutical composition or vaccine containing at least one (I), or its derivative, (II) or Ab.

ACTIVITY - Antiviral; anticancer.

No biological data is given.

MECHANISM OF ACTION - (I) induce a specific immune response; particularly they induce cytolysis, by cytotoxic T cells (CTL), of cells that express (I) associated with appropriate HLA molecules and induce secretion of cytokines (particularly interleukins -2 and -4, and gamma -interferon) by these CTL; vaccine.

USE - (I), their derivatives, nucleic acids encoding them and specific antibodies (Ab) are used, in compositions or vaccines, to treat or prevent diseases associated with human papilloma virus (HPV) infection, e.g. cervical or vulvar intraepithelial neoplasia and invasive cancer of the cervix uteri. Ab are also useful for in vitro diagnosis of these diseases.

ADVANTAGE - (I) may include CD4 epitopes recognized by T helper cells, and induces and maintains CD8+ T cells recognized by epitopes within (I).

ABSTRACTED-PUB-NO: FR 2794371A

EQUIVALENT-ABSTRACTS:

CHOSEN-DRAWING: Dwg.0/0

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L4: Entry 1 of 7

File: USPT

Dec 3, 2002

US-PAT-NO: 6489141

DOCUMENT-IDENTIFIER: US 6489141 B1

TITLE: Nucleic acid sequence and methods for selectively expressing a protein in a target cell or tissue

DATE-ISSUED: December 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Frazer; Ian</u> Hector	St. Lucia			AU
Zhou; Jian	late of Jindalee			AU

US-CL-CURRENT: 435/69.1; 435/320.1, 435/325, 435/455, 435/91.4, 435/91.41, 435/91.42, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
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☐ 2. Document ID: US 6365160 B1

L4: Entry 2 of 7

File: USPT

Apr 2, 2002

US-PAT-NO: 6365160

DOCUMENT-IDENTIFIER: US 6365160 B1

TITLE: Papillomavirus polyprotein constructs

DATE-ISSUED: April 2, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Webb; Elizabeth Ann	Eltham			AU
Margetts; Mary Brigid	Moonee Ponds			AU
Cox; John Cooper	Bullengarook			AU
<u>Frazer; Ian</u>	St. Lucia			AU
McMillan; Nigel Alan John	Woollahgabb			AU
Williams; Mark Philip	Annerley			AU
Moloney; Margaret Bridget Holland	Essendon			AU
Edwards; Stirling John	Coburg			AU

US-CL-CURRENT: 424/192.1; 424/186.1, 424/199.1, 424/204.1, 435/235.1, 435/320.1, 435/69.1, 435/69.7, 530/350, 536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KWIC
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☒ 3. Document ID: US 6306397 B1

L4: Entry 3 of 7

File: USPT

Oct 23, 2001

US-PAT-NO: 6306397

DOCUMENT-IDENTIFIER: US 6306397 B1

TITLE: Variants of human papilloma virus antigens

DATE-ISSUED: October 23, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Edwards; Stirling John	Northcote			AU
Cox; John Cooper	Bullengarook			AU
Webb; Elizabeth Ann	Eltham			AU
<u>Frazer; Ian</u>	St. Lucia			AU

US-CL-CURRENT: 424/192.1; 424/186.1, 424/204.1, 435/235.1, 435/69.1, 435/69.7,
536/23.1, 536/23.72, 536/24.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☒ 4. Document ID: US 6183745 B1

L4: Entry 4 of 7

File: USPT

Feb 6, 2001

US-PAT-NO: 6183745

DOCUMENT-IDENTIFIER: US 6183745 B1

TITLE: Subunit papilloma virus vaccine and peptides for use therein

DATE-ISSUED: February 6, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Tindle; Robert	Kenmore			AU
Fernando; Germain	Jamboree Heights			AU
<u>Frazer; Ian</u>	St. Lucia			AU

US-CL-CURRENT: 424/185.1; 530/350, 530/395, 530/403

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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☐ 5. Document ID: US 6013262 A

L4: Entry 5 of 7

File: USPT

Jan 11, 2000

US-PAT-NO: 6013262

DOCUMENT-IDENTIFIER: US 6013262 A

TITLE: Recombinant papilloma virus L1

DATE-ISSUED: January 11, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Frazer; Ian</u>	St. Lucia			AU
Zhou; Jian	Maywood	IL		

US-CL-CURRENT: 424/204.1; 435/235.1, 435/252.3, 435/320.1, 435/5, 435/69.1, 435/69.3,
435/7.1, 530/350, 530/403, 536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWC

☐ 6. Document ID: US 6004557 A

L4: Entry 6 of 7

File: USPT

Dec 21, 1999

US-PAT-NO: 6004557

DOCUMENT-IDENTIFIER: US 6004557 A

TITLE: Variants of human papillomavirus antigens

DATE-ISSUED: December 21, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Edwards; Stirling John	Caburg			AU
Cox; John Cooper	Bullengarook			AU
Webb; Elizabeth Ann	Eltham			AU
<u>Frazer; Ian</u>	St. Lucia.			AU

US-CL-CURRENT: 424/192.1; 424/186.1, 424/199.1, 424/204.1, 435/235.1, 435/320.1,
435/69.1, 435/69.7, 536/23.1, 536/23.72, 536/24.3

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 7. Document ID: US 5993821 A

L4: Entry 7 of 7

File: USPT

Nov 30, 1999

US-PAT-NO: 5993821

DOCUMENT-IDENTIFIER: US 5993821 A

TITLE: Modified papilloma virus L2 protein and VLPs formed therefrom

DATE-ISSUED: November 30, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
<u>Frazer; Ian</u>	St. Lucia			AU
Zhou; Jian	Jindalee			AU

US-CL-CURRENT: 424/204.1; 424/199.1, 435/235.1, 435/440, 435/69.1, 435/69.3, 536/23.72

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	KWIC
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